REMARKS

Compliance with Sequence Listing Requirements

The specification has been objected to for failing to comply with the requirements for Sequence Listings. More specifically, the Examiner asserts that the Brief Description of the Drawings and primer sequences of pages 68-69 need to be amended to refer to the SEQ ID NOS:. The specification has been amended to properly reference all relevant sequences in the Sequence Listing. No new matter has been added by these amendments. With regard to Figure 2, Applicants note that "PDGFRTM" is not an amino sequence, but rather the acronym for "platelet derived growth factor receptor transmembrane domain" as indicated on page 32 of the specification.

Enclosed herewith in full compliance to 37 C.F.R. §§1.821-1.825 is a Substitute Sequence Listing to be inserted into the specification as indicated above. The Substitute Sequence Listing in no way introduces new matter into the specification. Also submitted herewith in full compliance to 37 C.F.R. §§1.821-1.825 is a disk copy of the Substitute Sequence Listing. The disk copy of the Substitute Sequence Listing, file "2002-07-29 0147-0189P seq list.txt", is identical to the paper copy, except that it lacks formatting.

Restriction of the claims

Applicants acknowledge the Examiner's finality of the restriction requirement. Applicants affirm the election of claims 1-14, 18-20, 29, 36 and 38-42 and further reserve the right to file one or more divisional applications to any non-elected subject matter.

Objections to the Abstract

The Abstract of the Disclosure has been objected to for failing to be in proper form. The Abstract has been replaced with the attached Abstract of the Disclosure, which is in proper form.

Objections to the Drawings

The drawings have been objected to with the assertion that Figure 7 fails to depict the c-myc tag described in the specification. The specification has been amended to delete the erroneous reference to the c-myc tag in the legend of Figure 7. Support for this amendment may be found in Figure 7 and on pages 45 and 46, wherein the full description of the experiment corresponding to Figure 7 is contained. Withdrawal of the objection is respectfully requested.

Objections to the specification

The specification has been objected to for containing hyperlink information. The specification has been amended to delete the hyper

link references and replace the hyperlinks with web addresses that do not contain any embedded code. As such, the specification is in compliance with M.P.E.P. §608.05.

Objections to the claims

Claims 29 and 36 have been objected to as being dependent on non-elected claims. Claim 29 has been cancelled and claim 36 has been amended to depend only from elected claims. Withdrawal of the objection is respectfully requested.

Claims 18 and 36 have been objected to as being in improper multiple dependent form. Claims 18 and 36 have been amended to be in proper dependent form. The deleted subject matter of claims 18 and claim 36, in part, has been presented as new claims 43 and 44. Withdrawal of the objections is, therefore, respectfully requested.

Rejections under 35 U.S.C.§112, second paragraph

Claim 10 has been rejected under 35 U.S.C. §112, second paragraph with the assertion that "RIP" requires definition. Claim 10 has been amended to define "RIP" as "ribosomal-inactivating-protein."

Claim 19 has been rejected with the assertion that "binding domain as defined in claim 1" has no antecedent basis in claim 1. Claim 19 has

been amended to depend from claim 14. Claim 14 is drawn to a pathogenocide, thus claim 19 provides proper antecedent basis for all terms. In addition, claims 1 and 9 have been amended for clarity to recite "antibody or binding site thereof." Withdrawal of the rejection is respectfully requested.

Claims 20 and 36 have also been included in the rejection; however the Examiner gives no specific reason for the rejection of these claims. As such, Applicants assume that the inclusion of claims 20 and 36 was due to the dependency of these claims.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1-14, 18-20, 29, 36 and 38-42 have been rejected under 35 U.S.C. §112, first paragraph for lack of written description. More specifically, the Examiner asserts that the Applicants were only in possession of the eight fusion proteins listed on page 4 of the Office Action. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

Attached hereto is a third-party opinion of Dr. Paul Christou, which is being submitted under 37 C.F.R. §1.132. The Examiner asserts that the claims contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was

filed, had possession of the claimed subject matter." However, Dr. Christou, who is representative of one skilled in the art, as evidenced by his attached *curriculum vitae*, concluded from reading the specification that the present invention "provides fusion proteins having a binding domain, for example, an antibody, and a membrane localization domain that leads to membrane anchoring." In addition, Dr. Christou states that in his opinion, "the gist of the present invention is to anchor the binding domain of a fusion protein to the membrane of the plant cell and to thereby protect the plant from the pathogenic infection." Further, it is Dr. Christou's opinion that the Examples in the specification serve only to illustrate the above-discussed principle that the inventors were fully in possession of, and one skilled in the art would readily be able to, adapt this principle to other plant pathogens and desired targeting membrane domains. Thus, contrary to the assertion of the Examiner, the specification fully conveys to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed subject matter. Withdrawal of the rejection is, therefore respectfully requested.

Rejections under 35 U.S.C. §102(b)

Claims 1-12, 14, 18-20 and 41-42 have been rejected under 35 U.S.C. §102(b) as being anticipated by WO 96/09398 (hereinafter referred to as "WO '398"). The Examiner asserts that WO '398 discloses gene constructs

for fusion proteins comprising an antibody and a toxin/enzyme against fungi, nematodes, insects, bacteria and viruses. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997).

The present invention, as encompassed by claim 1, is drawn to a fusion protein having at least one binding domain comprising an antibody or binding site thereof that specifically recognizes an epitope of a plant pathogen; and a membrane localization sequence and/or motif that leads to membrane anchoring. WO '398 fails to disclose an membrane targeting sequences on page 6, line 17-27. As such, WO '398 fails to disclose every feature of the present invention and does not anticipate the present invention. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §103

Claims 1-12, 14, 18-20, 29, 36, 38 and 40-42 have been rejected under 35 U.S.C. §103 as being obvious over WO '398 combined with U.S. Pat. No. 5,374,548 (hereinafter referred to as "U.S. '548"). Further to the disclosure of WO '398, U.S. '548 is relied on for teaching fusion proteins utilizing a GPI (membrane localization) domain to target the

fusion protein to the cell surface membrane. The Examiner asserts that it would have been obvious to substitute the GPI domain of U.S. '548 in the fusion protein of WO '398. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

WO '398 discloses fusion proteins having an antibody sequence linked to the sequence of a toxic protein for use in plant protection. The Examiner asserts that it would be obvious to substitute the GPI domain of U.S. '548 in the fusion protein of WO '398. However, the Examiner's position is based on the erroneous interpretation of WO '398 as disclosing the inclusion of a membrane targeting sequence. However, as noted above, WO '398 fails to disclose the inclusion of a membrane targeting sequence, i.e. membrane localization sequence that leads to membrane anchoring.

The Examiner arbitrarily states that "It would have been obvious to one of ordinary skill in the art...to substitute the recombinant, generic GPI membrane localization sequence taught by the '548 patent in the recombinant fusion protein directed against a viral plant pathogen taught by the WO document." However, the Examiner fails to provide any evidence for why "it would be obvious" to use the GPI sequence with the fusion protein of WO '398.

To support an obviousness rejection based on a combination of references, the Examiner "must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to

combine them to render the claimed invention obvious."; In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783(Fed. Cir. 1992). The "factual question of motivation is material to patentability, and [cannot] be resolved on subjective belief and unknown authority." The Examiner must present requisite evidence in support of an assertion of motivation to combine references. In re Lee, 61 USPQ2d 1430, 1435 (Fed. Cir. 2002). The Examiner has failed to properly support the assertion of a motivation to combine the teachings of WO '398 and U.S. '548. As such, withdrawal of the rejection is respectfully requested.

Applicants further note that one skilled in the art would, in fact, have no motivation to combine the references. U.S. '548 pertains to a totally unrelated field to the present invention. U.S. '548 pertains to liposome targeting with therapeutic applications in mammals. One skilled in the art who was trying to improve plant defense mechanisms against pathogens would not look to a reference pertaining to liposome targeting in mammals. As such, there is no motivation to combine the references.

In addition, there would be no expectation of success based on the combined teachings of the references. There is no teaching, or any suggestion, in U.S. '548 that by fixing a fusion protein containing an antibody binding site in a cell membrane, the infectivity of a plant pathogen can be reduced. Example 1 of the specification (pages 50-51 and Table 2) disclose the successful production of a fusion protein

comprising an antibody directed against TMV and a membrane localization sequence that renders transgenic tomato plants resistant against TMV. There is no suggestion in or expectation from either prior art reference of the improved plant protection achieved with the present invention. As such, the present invention is not obvious over the combined references and withdrawal of the rejection is respectfully requested.

Claim 39 has been rejected under 35 U.S.C. §103 as being obvious over WO '398 combined with U.S. '548 and U.S. Pat. No. 5,698,679, (hereinafter referred to as "U.S. '679"). Further to the disclosures of WO '398 and U.S. '548, U.S. '679 is relied on for teaching a fusion protein using an immunoglobulin transmembrane domain as a membrane localization sequence. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

Claim 39 depends from claims 1 and 2, which are novel and non-obvious for the reasons discussed above. As such, claim 39 must also necessarily be novel and non-obvious.

In addition, as with U.S. '458, U.S. '679 pertains to a totally unrelated field such that one skilled in the art would have no motivation to combine the references or have any expectation of success if combined. U.S. '679 pertains to the modulation of an immune response with a fusion protein made from an immunoglobulin linked through the variable domain to an antigenic peptide, which is recognized by and

targeted to an antigen presenting cell. In a preferred embodiment, the fusion protein of U.S. '679 may include a membrane localization sequence to facilitate coupling of the fusion protein with a lipid-containing substrate such as a cell. This allows it to co-deliver other reagents with the fusion protein to the target cell. See column 10, lines 54-58. Thus, there is no disclosure in U.S. '679 regarding the improvement of plant defense against plant pathogens. Nor would one skilled in the art look to U.S. '679, which is from a totally unrelated field. As such, the invention of claim 39 is not obvious over WO '398 combined with U.S. '458 and U.S. '679 and withdrawal of the rejection is respectfully requested.

Claim 13 has been rejected under 35 U.S.C. §103 as being obvious over WO '398 combined with U.S. '548 and U.S. Pat. No. 5,876,950. Further to the disclosures of WO '398 and U.S. '548, U.S. '950 is relied on for teaching recombinant proteins labeled with a detectable marker, such as a flurophor, and methods of conjugating antibodies to the detectable marker. U.S. '950 is further relied on for teaching monoclonal antibodies conjugated to a therapeutic agent, such as a toxin. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

Claim 13 depends from claim 1, which is novel and non-obvious for the reasons discussed above. As such, claim 13 must also necessarily be novel and non-obvious.

In addition, as discussed above, the Examiner has failed to make the requisite showing of a motivation to combine WO '398 with U.S. '458. The present rejection of claim 13 over the additionally cited reference of U.S. '950 fails to compensate for the deficient showing. As such, the present invention of claim 13 is not obvious over the references.

There is further no motivation to combine WO '398 and U.S. '458 or any expectation of success if the references are combined because U.S. '458 pertains to a completely unrelated field to the present invention. U.S. '950 pertains to monoclonal antibodies specific for human gp39 and discloses that the anti-gp39 antibodies may be labeled with a fluorophor or linked to a toxin. See column 12, lines 11-21. Thus, U.S. '950 fails to make up for the deficiencies of U.S. '458 and to provide any motivation to combine the references or any expectation of success.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD (Reg. No. No. 40,069) at the telephone number of the undersigned below.

A marked-up version of the amended sections of the specification and claims is attached hereto.

Applicants request a three (3) month extension of time for responding to the office action. The required fee is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Gerald M. Murphy, Jr., #28,977

MaryAnne Armstrong, PhD #40,069

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

GMM/MAA
0147-0189P

Attachments: Marked-up version showing changes
Paper and Disk Copy of Substitute Sequence Listing
Declaration of Dr. Paul Christou

(Rev. 04/19/2000)

MARKED-UP VERSION SHOWING CHANGES

IN THE ABSTRACT

Please replace the Abstract of the Disclosure with the attached Abstract.

IN THE SPECIFICATION

The paragraph beginning at page 15, line 26, has been amended as follows.

--➤ toxins which kill the host cell where the pathogen is replicating and has penetrated the cytosol (Barbieri et al., 1993; Hartley et al., 1996; Madshus and Stenmark, 1992), for example (Ribosome inactivating proteins) RIPs which enter the cytosol and are among the most potent cytotoxins known. Ribosome-inactivation is achieved in all cases through the cleavage of an N-glycosidic bond between ribose and a specific adenine residue in the universally conserved sequence 5'-AGUACGA*GAGGA-3' (where A* indicates the target adenine) **(SEQ ID NO: 164)** located 250-400nt from the 3' end of 23S/25S/28S rRNAs (Endo and Tsurugi, 1987), (Hartley et al., 1996). Ribosomes depurinated in this manner are unable to bind the EF-2/GTP complex and protein synthesis is blocked at the translocation step (Montanaro et al., 1975). A single RIP molecule is able to depurinate 1000-2000 mammalian cell

ribosomes per min under physiological conditions (Eiklid et al., 1980; Endo and Tsurugi, 1988).--

The paragraph beginning at page 17, line 6, has been amended as follows.

-- In the constructs according to the invention, the antibody is preferably fused to a complete sequence of a toxic agent or a part thereof which still has activity, or which is still functionally active. Also, the chimeric protein may be encoded by nucleotide sequences on one or more constructs and may be assembled *in vivo* by the plant or expression organisms protein assembly and translation machinery. The chimeric protein can also be obtained by biochemical assembly or *in vitro* or *in vivo* assembly of the chimeric immunotoxin subunits using the cells endogenous protein assembly machinery. The antibody, antibodies or fragments thereof are fused directly to the toxic agent or linked by a flexible spacer which does not interfere with the structure or function of the two proteins. Such flexible linkers include copies of the (Glycine-Glycine- Glycine- Glycine-Serine)$_n$ linker **(SEQ ID NO: 165 - also referred to as Gly$_4$Ser),** where n is 1 to 4 or more copies of the linker unit, the Genex 212 and 218 linker and the flexible linker peptide of *Trichoderma reesi* cellobiohydrolase I (CBHI) (Turner et al., 1997), (Tang et al., 1996).--

The paragraph beginning at page 17, line 27, has been amended as follows.

-- The desired cellular location of the molecular pathogenicide, or any components thereof, can be achieved by using the appropriate cellular targeting signals, these include but are not limited to signal peptides, targeting sequences, retention signals, membrane anchors, post translational modifications and/or membrane transmembrane domains that target the protein to the desired organelle, desired membrane (plasma membrane, ER, Golgi, nucleus, chloroplast or vacuole) or desired membrane orientation (cytoplasmic or lumenal or plant cell membrane display) (Kim et al., 1997; Rose and Fink, 1987). Localisation sequences can be targeting sequences which are described, for example in chapter 35 (protein targeting) of L. Stryer *Biochemistry* 4th edition, W.H. Freeman, 1995. Proteins synthesised without a functional signal peptide are not co-translationally inserted into the secretory pathway and remain in the cytosol. Proteins that carry a signal peptide that directs them to the secretory pathway, which may include a transmembrane sequence or membrane anchor, will be targeted for secretion by default or reside in their target membrane organelles. Targeting signals can direct proteins to the ER, retain them in the ER (LYSLYS motif **(SEQ ID NO: 166)** and KDEL **(SEQ ID NO: 167)**), TGN 38, or will target proteins to cell organelles such as the chloroplasts, vacuole, nucleus, nuclear membrane, peroxisomes and mitochondria. Examples for signal sequences and targeting peptides are described in (von Heijne, 1985) (Bennett and Osteryoung, 1991) (Florack et al., 1994). In addition, the targeting signals may be cryptic and encoded by a host plant cell or heterologous eukaryotic cell proteins or animal proteins where the localisation is known and where the protein can be cloned. By constructing a fusion protein with this protein, a molecular pathogenicide can be targeted to the localisation of the protein without the need for identification of

the cryptic targeting signal. Suitable cryptic signals are those encoded by the resident Golgi enzymes. --

The paragraph beginning at page 31, line 15 has been amended as follows.

--These and other embodiments are disclosed and encompassed by the description and examples of the present invention. Further literature concerning any one of the methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries, using for example electronic devices. For example the public data base "Medline" may be utilised which is available on the Internet, for example **at the following World Wide Web domain site address "ncbl.nlm.nih.gov/PubMed/medline.html". Further databases and addresses such as those found at the World Wide Web domain site addresses "ncbi.nlm.nih.gov", "infoblogen.fr", "fmi.ch/biology/research tools.html", and "tigr.org" are known to the person skilled in the art and can also be obtained using search engines such as "lycos.com"** ~~for example under http://www.ncbl.nlm.nih.gov/PubMed/medline.html. Further databases and addresses such as http//www.ncbi.nlm.nih.gov/, http://www.infoblogen.fr/, http://fmi.ch/biology/research_tools.html, htt://www.tigr.org are known to the person skilled in the art and can also be obtained using, e.g. http://www.lycos.com.~~ An overview of patent information in biotechnology and a survey of relevant sources of

patent information useful for retrospective searching and for current awareness if given in Berks, TIBTECH 12 (1994) 352-364.--

The paragraph beginning at page 32, line 20, has been amended as follows.

-- **Figure 3** shows example constructs for molecular pathogenicide display facing the cell cytoplasm. 35SS: 35S promoter from Cauliflower Mosaic Virus with duplicated enhancer; CHS 5'-UT: chalcone synthase 5' untranslated region; VL: Variable domain of the parental monoclonal antibody 24 light chain; VH: Variable domain of the parental monoclonal antibody 24 heavy chain; Linker 1: 14 amino acid linker (Genex 212) sequence; Linker 2: 10 amino acid linker (Gly4Ser)2 sequence **(SEQ ID NO: 168)**; Term: termination sequence from Cauliflower mosaic virus.--

The paragraph beginning at page 34, line 7, has been amended as follows.

--**Figure 7** shows a cDNA construct for targeting and expression of scFv24 on plant cell membranes. CDNAs of mAb24 variable light (V_L) and heavy chain (V_H) domains connected by a 14 amino acid linker were fused to the human TcRβ transmembrane domain and cloned into *EcoRI* and *XbaI* restriction sites of the plant expression vector pSS (33). The DNA sequence of the *EcoRI/XbaI* fragment from pscFv24-TcRβ is depicted in SEQ ID NO:3. 35SS = double enhanced CaMV-35S promoter; CHS-5'-UT = 5'

untranslated region of the chalchone synthase; LP = signal sequence of the murine mAb24 light chain; ~~*c-myc = c-myc-epitope tag;*~~ TM = transmembrane domain; TcaMV = CaMV termination sequence.--

The paragraph beginning at page 36, line 26 has been amended as follows.

--**Figure 14** **(SEQ ID NO: 19)** Molecular pathogenocide based on a single chain (scFv24) fusion to *E. coli* RNAse. The two domains of the pathogenocide were connected by a short Gly-Gly-Gly-Ser **(SEQ ID NO: 165)** linker peptide. This set up can be modified in multiple ways by using different scFv antibodies binding to structural and nonstructural viral target proteins, other RNAase genes or domains thereof fused to either the N- or C-terminus of any selected scFv cDNA.--

The paragraph beginning at page 38, line 24 has been amended as follows.

--**Figure 21** shows the amino acid residues of two selected scFv binding to the 30K movement protein of TMV obtained by phage display using GST-30K immunized mice for PCR-based amplification of V_H- and V_L-fragments. ScFv 30-1 **(SEQ ID NO: 29)** = 30K specific scFv No.1, scFv 30 -2 **(SEQ ID NO:30)** specific scFv No.2. Amino acid residues were derived from cDNA-sequencing of the respective phage derived scFv-cDNA clones as described (Figure 19).--

The paragraph beginning at page 39, line 4 has been amended as follows.

--**Figure 23** shows amino acid sequences derived from the cDNA sequences of antiviral scFv-antibodies obtained by hybridoma rescue (Figure 24) directed against the 3a movement protein of CMV **(SEQ ID NO: 113)** (23a), a component of the TMV replicase **(SEQ ID NO: 114)** 23b, 54K of TMV) and a plant virus minimal protein **(SEQ ID NO: 115)** (23c, 3 min of PLRV).--

The paragraph beginning at page 39, line 18 has been amended as follows.

--**Figure 25:** Epitope mapping of three different antiviral antibodies namely (a) mAb 29 (see Example 1), (b) scFv 54-1 (Example 6, Figure 23b, Figure 29) and (c) scFv 3a-2 (Example 6, Figure 23a). Sequences were obtained from phage ELISA positive clones after the third round of biopanning using two peptide display libraries (Cortese et al. (1995) Curr. Opin. Biotechno. 6, 73-80). Resulting sequences **(SEQ ID NOS: 116-156)** were aligned and the consensus epitope was determined. In each case the epitope could be mapped within the parental sequence of the different viral sequences analysed.--

The Table on pages 68 and 69 has been amended as follows.

Name	Specificity according to Kabat (1991)	Overhang/ Enzyme Region	Annealing region
MPD VHF 1 **(SEQ ID NO: 31)**	Mu V_H IA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAK GTR CAG CTT CAG GAG TCR GGA
MPD VHF 2 **(SEQ ID NO: 32)**	Mu V_H IB Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG GTG MAG CTG AWG GAR TCT GG
MPD VHF 3 **(SEQ ID NO: 33)**	Mu V_H IIA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTC CAG CTR CAR CAR TCT GGA CC
MPD VHF 4 **(SEQ ID NO: 34)**	Mu V_H IIA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG GTW CAG CTS CAG CAG TCT G
MPD VHF 5 **(SEQ ID NO: 35)**	Mu V_H IIB Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	SAG GTC CAR CTG CAG SAR YCT GGR
MPD VHF 6 **(SEQ ID NO: 36)**	Mu V_H IIC Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTT CAG CTG CAG CAG TCT GGG
MPD VHF 7 **(SEQ ID NO: 37)**	Mu V_H IIIA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAR GTG AAG CTG GTG GAR TCT GGR
MPD VHF 8 **(SEQ ID NO: 38)**	Mu V_H IIIB Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTG AAG STY MTC GAG TCT GGA
MPD VHF 9 **(SEQ ID NO: 39)**	Mu V_H IIIC Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAR GTG AAG CTK GAK GAG WCT GR
MPD VHF 10 **(SEQ ID NO: 40)**	Mu V_H IIID Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAV GTG MWG CTK GTG GAG TCT GGK
MPD VHF 11 **(SEQ ID NO: 41)**	Mu V_H IIID Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTG CAR CTK GTT GAG TCT GGT G
MPD VHF 12 **(SEQ ID NO: 42)**	Mu V_H VA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	SAG GTY CAG CTK CAG CAG TCT GGA
MPD VHF 13 **(SEQ ID NO: 43)**	Mu V_H 1 Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG ATC CAG TTG GTG CAG TCT GGA
MPD VHF 14 **(SEQ ID NO: 44)**	Mu V_H 2 Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG GTS CAC STG RWG SAG TCT GGG
MPD VHF 15 **(SEQ ID NO: 45)**	Mu V_H 3 Front	CAG GTS CAC STG RWG SAG TCT GGG	CAG GTT ACT CTR AAA GWG TST GGC C
MPD VHF 16 **(SEQ ID NO: 46)**	Mu V_H 4 Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAT GTG AAC TTG GAA GTG TCT GG

Name	Specificity according to Kabat (1991)	Overhang/ Enzyme Region	Annealing region
MPD VLF1 **(SEQ ID NO: 47)**	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG MTG WCH CAG TCT CCA
MPD VLF2 **(SEQ ID NO: 48)**	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT CAG ATG ATT CAG TCT CC
MPD VLF3 **(SEQ ID NO: 49)**	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTT CTC WHC CAG TCT CC
MPD VLF4 **(SEQ ID NO: 50)**	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG MTG WCH CAG TCT CAA
MPD VLF5 **(SEQ ID NO: 51)**	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAT RTT KTG ATG ACC CAR RCK GCA
MPD VLF6 **(SEQ ID NO: 52)**	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAT RTT KTG ATG ACC CAR RCK CCA
MPD VLF7 **(SEQ ID NO: 53)**	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG ATG ACC CAR BHT G
MPD VLF8 **(SEQ ID NO: 54)**	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAT ATT KTG ATG ACC CAR AYT CC
MPD VLF9 **(SEQ ID NO: 55)**	Mu kappa V_L III Front	CAT GCC ATG ACT CGC GGC GCG CCT	RAM ATT GTG MTG ACC CAA TYT CCW
MPD VLF10 **(SEQ ID NO: 56)**	Mu kappa V_L IV Front	CAT GCC ATG ACT CGC GGC GCG CCT	SAA AWT GTK CTS ACC CAG TCT CCA
MPD VLF11 **(SEQ ID NO: 57)**	Mu kappa V_L V/VI Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAY ATY CAG ATG ACM CAG WCT AC
MPD VLF12 **(SEQ ID NO: 58)**	Mu kappa V_L V/VI Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAY ATY CAG ATG ACH CAG WCT CC
MPD VLF13 **(SEQ ID NO: 59)**	Mu kappa V_L V/VI Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG ATG ACT CAG GCT AC
MPD VLF14 **(SEQ ID NO: 60)**	Mu lambda V_L 1 Front	CAT GCC ATG ACT CGC GGC GCG CCT	CAR SYT GTK STS ACT CAG KAA T
MPD VLF15 **(SEQ ID NO: 61)**	Mu lambda V_L 1 Front	CAT GCC ATG ACT CGC GGC GCG CCT	CAR SYT GTK STS ACT CAG KCA T
MPD VHB1 **(SEQ ID NO: 62)**	Mu V_H J_H 1 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA SMG TRG TC
MPD VHB2	Mu V_H J_H 2 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA SRG TRG TG

Name	Specificity according to Kabat (1991)	Overhang/ Enzyme Region	Annealing region
(SEQ ID NO: 63)			
MPD VHB3 **(SEQ ID NO: 64)**	Mu V_H J_H 3 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA SCA GRG TC
MPD VHB4 **(SEQ ID NO: 65)**	Mu V_H J_H 4 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA STG AGG TT
MPD VHB5 **(SEQ ID NO: 66)**	Mu V_H J_H 4 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA STG ARA TT
MPD VLB1 **(SEQ ID NO: 67)**	Mu kappa V_L I/II/IV back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG TTT CAG YTC CAR YTT
MPD VLB2 **(SEQ ID NO: 68)**	Mu kappa V_L I/II/IV back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG TTT KAT YTC CAR YTT
MPD VLB3 **(SEQ ID NO: 69)**	Mu kappa V_L IV back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG TTT BAK YTC TAT CTT TGT
MPD VLB4 **(SEQ ID NO: 70)**	Mu kappa V_L I/II/V back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG AGC MCG TTT TAT TTC CAA MKT
MPD VLB5 **(SEQ ID NO: 71)**	Mu lambda V_L back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	CTG RCC TAG GAC AGT SAS YTT GGT

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The Sequence Listing filed on January 31, 2000 has been replaced with the substitute Sequence Listing enclosed herewith.

IN THE CLAIMS

Claim 29 has been cancelled.

Claims 1, 9, 10, 18, 19 and 36 have been amended as follows.

1. (Twice Amended) A fusion protein comprising

(a) at least one binding domain comprising an antibody or binding site **thereof** that specifically recognizes an epitope of a plant pathogen; and

(b) a membrane localization sequence and/or motif that leads to membrane anchoring.

9. (Twice Amended) The fusion protein of claim 2 wherein the toxin is an enzyme or a viral structural or non-structural protein or a binding domain comprising an antibody or binding site **thereof** that specifically recognizes an epitope of a plant pathogen.

10. (Amended) The fusion protein of claim 9 wherein said enzyme is chitinase or glucanase, glucose oxidase, superoxide dismutase, DNAse or RNAse or **ribosomal-inactivating-protein ("RIP")** ~~RIP~~ or lipase or active fragments thereof either singly or in any combination(s).

18. (Twice Amended) The fusion protein of claim 1 ~~or the pathogenocide of claim 14~~, wherein said binding domain(s) and/or said further domain(s) are capable of self assembly in vivo.

19. (Amended) ~~A~~ **The** pathogenocide **of claim 14 the antibody or binding site thereof** ~~comprising at least one binding domain as defined in any one of claims 1 to 6, wherein at least one of said binding~~

~~domains~~ specifically recognizes a viral movement and/or replicase protein.

36. (Amended) A kit comprising the fusion protein of ~~any one of claims 1 to 13 or 18~~ **claim 1 or**~~,~~ the pathogenocide of ~~any one of claims 14 to 20~~ **claim 14**, ~~the polynucleotide of claim 21, the vector of claim 22, 23, 25 or 26, the composition of any one of claims 24 to 26 or the molecular pathogenocide of claim 29~~.

New claims 43 and 44 have been added.